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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/996,569	11/30/2001	Daniel R. Soppet	PF201D2	3798

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EXAMINER	
SPECTOR, LORRAINE	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 12/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

SM.

Office Action Summary	Application No.	Applicant(s)	
	09/996,569	SOPPET ET AL.	
	Examiner	Art Unit	
	Lorraine Spector, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,8,10-17 and 21-100* is/are pending in the application.

4a) Of the above claim(s) *1,8 and 11-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10 and 21-100* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,8,10-17 and 21-100* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11/30/2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11/30/2001* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Part III: Detailed Office Action

Restriction Requirement:

Applicant's election with traverse of Invention III in the paper filed 9/12/2003 is acknowledged. The traversal is on the ground(s) that (1)the groups of inventions are not independent, and (2) the examination of the entire application would not constitute a burden to search. This is not found persuasive because with respect to point (1) above, the inventions are distinct as noted in the last Office Action, as shown by the distinctness described therein. Applicant's attention is directed to MPEP 806.05. With respect to point (2) above, contrary to applicants' assertion that any search of the prior art in regard to group III will reveal whether any prior art exists as to the other Groups, a search is directed to references which would render the invention obvious, as well as references directed to anticipation of the invention, and therefore requires a search of relevant literature in many different areas of subject matter.

The requirement is still deemed proper and is therefore made FINAL.

Claims 10 and 21-100 are under consideration. Claims 1, 8, 11-17 and 19 are withdrawn from consideration as being drawn to a non-elected invention.

Formal Matters:

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claims 31, 32, 53, 54, 68, 69, 90, 91, 99 and 100 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The Examiner is unaware of any antibodies meeting the limitations of the independent claims that would not be suitable for use in western blotting or ELISA procedures.

Claim 10 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claim depends from claim 8, which is drawn to a patentably distinct invention; the antibody does not further limit the protein to which it binds.

Applicant is reminded of the proper content of an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof. If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

Where applicable, the abstract should include the following:
(1) if a machine or apparatus, its organization and operation;
(2) if an article, its method of making;
(3) if a chemical compound, its identity and use;
(4) if a mixture, its ingredients;
(5) if a process, the steps.

Extensive mechanical and design details of apparatus should not be given.

The abstract of the invention if objected to because there is no reference therein to the claimed antibodies. Correction is required.

Applicant is advised that should claims 23, 42, 49, 60, 79 or 83 be found allowable, claims 26, 44, 46, 63, 81, and 86, respectively, will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

The disclosure is objected to because of the following informalities:

The brief description of the drawings should be amended to refer to each separately numbered figure, e.g. Figures 1A and 1B. See §37 CFR 1.74.

Appropriate correction is required.

This application lacks formal drawings. The informal drawings filed in this application are acceptable for examination purposes. When the application is allowed, applicant will be required to submit new formal drawings.

Objections and Rejections under 35 U.S.C. §101:

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 10 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim is directed to "An antibody", without reference to isolation or other activity that would serve to show the hand of the inventor. Accordingly, the claim reads on products of nature, and is therefore non-statutory.

Objections and Rejections under 35 U.S.C. §112:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10, 27, 50, 60, 64, 76, 83 and 87 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 10 is drawn to antibodies against the polypeptide of claim 8. Claim 8, which is non-elected, recites "fragments, analogs, and derivatives" as being included in the scope of the claim. To the extent that such "analogs and derivatives", which are further defined as encompassing functional equivalents at page 11 of the specification, include epitopes not found in the disclosed protein, there is no written description in the specification as originally filed of the structure of such proteins, and therefore of antibodies that bind to such.

Claims 27, 50, 64 and 87 recite that the protein to which the claimed antibodies bind is glycosylated. As there is no disclosure of the glycosylation state of the protein as it occurs in nature, and further, as proteins may be artificially glycosylated, to the extent that the glycosylation is other than that which would occur in nature, and further, to the extent that such glycosylation would either create epitopes not found in the disclosed protein or hide epitopes, there is no written description of the epitopes so created or affected, and hence of antibodies that bind specifically to the protein in a glycosylated state.

Claims 60, 76 and 83 recite a "mature" polypeptide. There is no disclosure in the specification as originally filed of the "mature" polypeptide, nor identification of the sequence that would be cleaved to make the "mature" polypeptide. Accordingly, there is no written description of antibodies that would bind to said "mature" polypeptide.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was

in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

With the exception of the non-glycosylated proteins, or the proteins having the disclosed sequence as produced recombinantly by cells described in the disclosure, the skilled artisan cannot envision the detailed chemical structure of the encompassed antibodies, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

Therefore, only antibodies to the protein having the specifically disclosed sequence, or produced by the deposited cell line, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 58-94 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The deposit of biological organisms is considered by the Examiner to be necessary for enablement of the current invention (see 37 C.F.R.§1.808(a)). This determination is made because the deposited material must be available to practice the invention as it is claimed. Examiner acknowledges the deposit of organisms under ATCC accession number 97186 under terms of the Budapest Treaty on International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure in partial compliance with this requirement. However, in order to be fully compliant with the requirement, applicants must state that all restrictions on the

availability to the public of the deposited material will be irrevocably removed upon the granting of a patent. See 37 C.F.R.§1.808(a)(2).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10, 35, 36, 43, 57, 72, 73, 80, 89, 94 and 95-100 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 is indefinite as the metes and bounds of "analogs and derivatives" as recited in claim 8 cannot be determined, and accordingly the metes and bounds of the antibodies encompassed by claim 10 cannot be determined. Further, as there is inadequate written description of the claimed antibody, for reasons above, the metes and bounds of the claim cannot be determined.

Claims 35, 57, 72 and 92 are drawn to incomplete methods. There is no nexus between step (a), in which the sample is contacted with the antibody or fragment thereof, and step (b), in which the protein is detected.

Claims 43 and 80 are indefinite because the claims require that the antibody or fragment be "obtained from an animal", and also require that said antibody be "chimeric" or "humanized", neither of which antibodies can be obtained from animals. Further, while not indefinite, it is noted that the independent claims from which they depend also stated that the "fragment thereof" is "obtained from an animal", which may not be applicant's intent. It is suggested that the independent claims be amended to indicate that it is an "antibody" which is obtained from an animal, "or a fragment of said antibody", which would encompass post-isolation cleavage as well as naturally occurring fragments.

Claim 89 is indefinite as monoclonal antibodies are not chimeric or humanized.

Claim 95 is indefinite because (a) there is no nexus between the recited polynucleotide and the PTH receptor expressed on the cells.

The remaining claims are indefinite for depending from an indefinite claim.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 10, 21-27, 29, 31-50, 53-64, 66, 68-79, 81-87, 90-100 are rejected under 35 U.S.C. 102(e) as being anticipated by Segre et al., U.S. Patent Number 5,840,853. This rejection is based upon the effective filing date of the patent, which is *at least* 4/6/1992.

Segre et al. disclose peptides derived from parathyroid hormone receptor. In particular, SEQ ID NO: 7 of Segre et al. is 100% identical to residues 245-258 of SEQ ID NO: 2 of the instant application, a match of 14 contiguous amino acids out of the total length of 19 amino acids for the peptide of Segre et al. Both monoclonal and polyclonal antibodies to the peptide are disclosed, see claims 8-10, and the paragraph bridging columns 3-4, as well as the paragraph bridging columns 21-22, which additionally discloses hybridoma cells. Assays consistent with the claims are disclosed at column 21. It is noted that the first six residues that match are in an extracellular region of the protein, see Watson et al., "The G-Protein linked receptor factsbook",

Academic Press, San Diego, 1994, at page 232. As antibodies Segre's SEQ ID NO: 7 would bind to larger proteins comprising that sequence, the claims are anticipated by Segre et al.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 30, 52, 67, 80, and 89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Segre et al., U.S. Patent Number 5,840,853, in view of U.S. Patent Number 5,565,332 (Hoogenboom et al.), or in view of U.S. Patent Number 4,946,778 (Ladner et al.).

The teachings of Segre et al. are summarized above. Segre does not teach single chain, humanized, or fragment antibodies.

Hoogenboom et al. disclose humanized antibodies and methods of making such. At col. 1 lines 16-30 they disclose the advantages of such as being overcoming the problem of elicitation of anti-globulin response when a non-human antibody is administered to a human. See also col. 3 lines 8-15 in this regard. At column 2 lines 57+, they disclose that antibody fragments can perform the function of whole antibodies, and set forth single chain antibodies as being examples of antibody fragments.

Ladner et al. teach the construction of single chain antibodies . The stated advantages of such as enumerated at column 3 lines 32-48 include smaller size, greater stability, lower cost, lower immunogenicity, etc.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to substitute the antibodies of Segre et al. into the single chain or humanized antibodies of Ladner et al. or Hoogenboom et al. to attain the known and expected advantages of such as set forth by the secondary references and as referred to above.

Claims 28, 51, 65, and 88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Segre et al., U.S. Patent Number 5,840,853, in view of U.S. Patent Number 5,298,419)Masuho et al.)

The teachings of Segre et al. are summarized above. Segre does not teach human antibodies.

Masuho teaches the desirability of using human, rather than mouse monoclonal antibodies for the treatment of humans. Specifically, at column 2, they state:

> However, unfortunately, they (mouse monoclonal antibodies)are unsuited for the tasks of prevention of HIV infection and treatment of established disease (ARC and AIDS), since these MCAs are mouse proteins, and therefore they are recognized as foreign by the human immune system if they are administered to the human body. As a result, not only would the MCA activity be inhibited by the anti-mouse MCA antibodies that would be produced by the human immune system, but anaphylactic side effects would also occur. Therefore, it is clear that for the prevention and treatment of HIV infection in man, it is necessary to develop an MCA of human origin, rather than an MCA of mouse origin.

In the following paragraph, they disclose that production of human monoclonal antibodies was routine in the art.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to substitute the antibodies of Segre et al. into the human antibodies of Masuho et al. to attain the known and expected advantages of such as set forth by the secondary reference and as referred to above.

Advisory Information:

No claim is allowed.

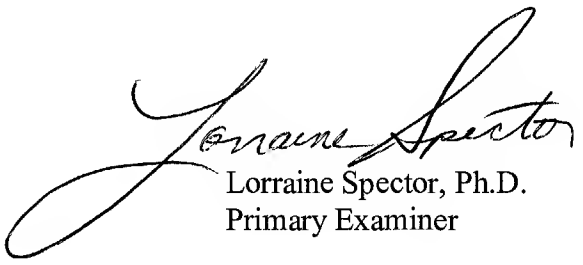
Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 5:30 P.M. ***Effective 1/21/2004, Dr. Spector's telephone number will be 571-272-0893.***

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary L. Kunz, at (703)308-4623. ***Effective 1/21/2004, Dr. Kunz' telephone number will be 571-272-0887.***

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 872-9306 (before final rejection) or (703)872-9307 (after final). Faxed draft or informal communications with the examiner should be directed to (703) 746-5228. ***Effective 1/21/2004, Dr. Spector's fax number will be 571-273-0893.***



Lorraine Spector, Ph.D.
Primary Examiner

12/09/2003